

10.5 PLACENTA
TESTIS
SEMINAL VESICLE
OVARY
OVIDUCT
UTERUS
BRAIN
THYMUS
HEART
LUNG
KIDNEY
ADRENAL
SPLEEN
LIVER
INTESTINE
PANCREAS

FIG. 1A

8.5
10.5
12.5
14.5
16.5
18.5

FIG. 1B

| | | |
|------|---|------|
| 1 | TTCAAGCCCTCAGTCAGTTGTGCGGGAGAAAGGGGGCGGTGCGGCTTTCTCTTCAAGAA | 60 |
| 61 | CGAGTTATTTTCAAGCTGAGCTGGAGACGGTGCAAGTCTGGACACGGGAGCACTTCCAC | 120 |
| 121 | TATGGGACTGGATACAGACACAGCCCGGGGACTTCAAGACACTCAGACTGAGGAGAAA | 180 |
| 181 | GCCCTGCCCTGCTGCTGCTGCTGCTGCCACCGCTGCCCTCTGAAGACCCACTCCCTT | 240 |
| 241 | TCATGGTTTTCCTGCCAAGCCAGAGGACCTTCGCTGCTACGGCCTTTCTCTGTGTGT | 300 |
| 301 | CATTACGGGCTGGCCAGAGGATGAGACTCCCCAAACTCCTCACTCTTTTGCTGTGGCAC | 360 |
| 361 | CTGGCTTGGCTGGACCTGGAACCTCATCTGCACCTGTGCTGGGTGCCCTGACTTAGGACAG | 420 |
| 421 | AGAACCCACGGGCCAAGCCAGGGTTGACCAAGCGGAGGCCAAGGAGAGGCCACCCCTG | 480 |
| 481 | GCCAGGAATGCTTTAGGCCAGGGGTCTATCTATGTGTGGGGCCACCAATGCCAGG | 540 |
| 541 | GCCAAGGGAAGCTCTGGCAGACACAGGCCAAGAGGATGAACCCAGAAAAGATGCCCCC | 600 |
| 601 | AGATCCGGTGGCTCTGAAACCAAGCCAGGACCCCTCTTCCCAGACTAGACAGGCTGCAGCC | 660 |
| 661 | CGGACTGTAACCCCAAGGACAGCTTCTTGGGGCAAGCATCTTCAAAAGCAGGATCT | 720 |
| 721 | GCCCCAGCTCCTTCTGTAAGAAGACCAAGGAGCCTGGGACCCCTCGAGAGCCCCAAG | 780 |
| 781 | GAGCCGTTCCGGCCGCCCCATCACACCCACGAATACATGCTCTCCCTGTACAGGACG | 840 |
| 841 | CTGTCCGATGCTACAGAAAGGAGGTAAACAGCAGCGTGAAGTTGGAGGCTGGCCTGGCC | 900 |
| 901 | LSDADARKGGNSSVKLEAGLA | 960 |
| 961 | CAGAGGTACGTMTTGACATCAGTGCCTTGGAGAAGGATGGGCTGTTGGGGCTGAAC TG | 1020 |
| 1021 | CGGATCTTACGGAAGACCCCTTGGACGTGGCCCAAGCCAGCGGTCCCCAGTAGCGGGCGG | 1080 |
| 1081 | GTTGCCCAACTGAAGCTGTCCAGCTGCCCCAGCGGCCGCGCAGCCCTTGCTGGAT | 1140 |

FIG. 2A

1141 GTGCGTCCGTGCGCCGCTGGATGGATCTGGCTGGGAGGTGTTGACATCTGGAAGCTC 1200
V R S V P G L D G S G W E V F D I W K L
1201 TTCCGAAATTTAAGAACTCAGCGCAGCTGTGCCCTGGAGCTGGAGGCCTGGGAACGGGGC 1260
F R N F K N S A Q L C L E L E A W E R G
1261 CGGCGCGTGGACCTCCGTGCGCTGGCTTTGAACGCACTGCCCGACAGGTCCACGAGAAA 1320
R A V D L R G L G F E R T A R Q V H E K
1321 GCCTGTTCCTAGTGTGTTGGTCGTACCAAGAAACGGGACCTGTTCTTTAATGAGATTAAAG 1380
A L F L V F G R T K K R D L F F N E I K
1381 GCCGCTCTGGCCAGGATGACAAGACTGTGTATGAATATTGTTTCAGCCAGCGCGGAAA 1440
A R S G Q D D K T V Y E Y L F S Q **R R K**
1441 CGCGGGCCCCATTGGCCAAATCGCCAGGCAAGCGACCCAGCAAGAACCTCAAGGCTCGC 1500
R R A P L A N R Q G K R P S K N L K A R
1501 TGCAGTCGCAAGGCCCTTGCCATGTCAACTTCAAGGACATGGGCTGGGACGACTGGATCATC 1560
C S R K A L H V N F K D M G W D D W I I
1561 GCACCTCTTGAGTATGAGGCCCTTCCACTGCGAAGGACTGTGTGAGTTCCCTTGGCTCC 1620
A P L E Y E A F H C E G L C E F P L R S
1621 CACTTGGAGCCCCACAAACCAGCAGTCATTACAGACCCTAATGAACCTCTATGGACCCTGAA 1680
H L E P T N H A V I Q T L M N S M D P E
1681 TCCACACCAACCCTGTTGTTGTGTCCTACACGGCTGAGTCCCTATTAGCATCCTCTTCATC 1740
S T P P T C C V P T R L S P I S I L F I
1741 GACTCTGCCAACAAACGTGGTGATATAAACAGTACGAGGACATGGTCGTGGAATCTTGTGGC 1800
D S A N N V V Y K Q Y E D M V V E S C G
1801 TGCAGGTAGCAGCACCGGCCCCACCTGTCTTCCAGGCTGGCACATCCAGAGACTACCCCT 1860
C R *
1861 CTACAGGTTCTCTGGAGTAACAGAGAGCCCTGTGAAGCTGCTGCCCGAAGTTTCTTGGCAGC 1920
1921 CTGCAGGAAAGAGTTCTCAGCAGGCTTACTCTCTGGATGTGATCTGGACTAAGAGATCA 1980
1981 CCTCTGAAGATTCTCTGCCCAAGGAACAGACTCTGAGTGGGCCCTGGGGCTCAGGAAAGGT 2040
2041 GTTCTTAATGAGATTCAGTTCACCATCTCTCTCCCGGGCCGAGACCTTCAATTTCTCT 2100
2101 CCAGACTCTCCAGAGAAGTGTAGCTATATCTTAAGCTCTTTAAGGAGAGCTGTCTCCT 2160
2161 CCTGAATCACCTTTGTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 2220
2221 GCAAAGAAGGGGAAAGGGCTTGGGCAGGGGTGAAGAGAAGAGTATGAGCCTAATTAGACT 2280
2281 GTTAGATTAAATGTACATCGATGACATAAAAGCTGAATCTTTCATGGCT 2329

FIG. 2B

GDF-1
 GDF-3
 GDF-5
 GDF-9
 BMP-2
 BMP-4
 Vgr-1
 Op-1
 BMP-5
 BMP-3
 MJS
 Inhibin
 Inhibin
 Inhibin
 Inhibin
 TGF- β_1
 TGF- β_2
 TGF- β_3

RLRRHTEPRVEGVPVGTGTRRRLLHVSF-REVGVHRRWVIAPRGFLANFCQGTICALPETLRGPGGPP
 RKRRAAISVPKGF CRNFCHRRHQLFINF-QDLGWKHWIAPKGFMANYYCHGECFPFSMTTYLNS---
 PLANRQGRPSKNLKARCSRKALHVNF-KDMGWDDWI IAPLEYEAFHCEGLCEFLRSHLEP---
 SFNLSEYFKQLFPQNECELHDFRLSF-SOLKWDNWI VAPHRYNPRYCKGDCPRAVRHRYGS---
 REKROAKHKQRKRLKSSCKRHPLYVDF-SDVGWNDWI VAPPGYHAFYCHGECPEPLADHLNS---
 KRSPKHSQRARKKNKNCRRHSLYVDF-SDVGWNDWI VAPPGYQAFYCHGDCFPPLADHLNS---
 SRGSGSDYNGSELKTA CKKHEL YVSF-QDLGWQDWI IAPKGYAANYCDGEC SFPLNAHMA---
 LRMANVAENSSDQROACKKHEL YVSF-RDLGWQDWI IAPEGYAAAYCEGECAPPLNSYMA---
 SRMSSVG DYNTSEQOACKKHEL YVSF-RDLGWQDWI IAPEGYAAFYCDGEC SFPLNAHMA---
 EQTLKARRKQWIEPRNCARRYLKVDF-ADJGWSEWI ISPKSFDAYYCSGACQFPMPKSLKPS---
 GPGRAQRSAGATAADGPGCALRELSVDL----RAERSVLIPETYQANNQGVGWQPSDRNPRY---
 ALRLLRQPPEEPAAHANCHRVALNISF-QELGWERWIVYPPSFIFHYCHGGCGGLHPNLSLPV-
 HRRRRRGLECDGKV-NICCKQFFVSF-KDIGWNDWI IAPSGHYANYCEGECPSHIAGTSGSSL-
 HRI RKRDGLEDGRT-NLCCRQOFFIDE-RLJGNDWI IAPTGYGYNYCEGSCPAYLAGVPGSAS-
 HRRALDTNYCESSTENKCCVRQLYIDFKDLGWK-WIHEPKGYHANFOLGPOPIWSLD-----
 KKRALDAAYCFRNQVDNCCRLPLYIDFKRDLGWK-WIHEPKGYNANFQAGACPYLWSSD-----
 KKRALDTNYCERNLEENCCVRPLYIDFKRDLGWK-WVHEPKGYANFQSGGQPYLR SAD-----

GDF-1 ALNHAIVQLVNS---VNSKIPKACCV--PTELSAISMLYL--DENEKVVLNKYQDMVVEGCGGR
 GDF-3 -TNHAIVQTLVNS---VNSSIPKACCV--PTELSAISMLYL--DEYDKVVLKNYQEMVVEGCGGR
 GDF-5 -SNYAFMQALMHM---ADPKVPKAVCV--PTKLSPI SMLYQ--DSDKNVILRHVEDMVVDECGCG
 GDF-9 -TNHAVIQTLMNS---MDPESTPTTCV--PTRLSPI SILFI--DSANNVYKQYEDMVVESCGCR
 -PVHTMVQNI IYE--KLDPSVPRPCV--PGKYSPLSVLTI--EPDGSIAKEYEDMIA TRCTCR
 BMP-2 -TNHAIVQTLVNS---VNSKIPKACCV--PTELSAISMLYL--DENEKVVLNKYQDMVVEGCGGR
 BMP-4 -TNHAIVQTLVNS---VNSSIPKACCV--PTELSAISMLYL--DEYDKVVLKNYQEMVVEGCGGR
 Vgr-1 -TNHAIVQTLVHL--MNPEYVPKPCA--PTQLNAISVL YF--DDSNVILKKYRNMMVVRACGCH
 OP-1 -TNHAIVQTLVHF--INPETHVPKPCA--PTQLNAISVL YF--DDSNVILKKYRNMMVVRACGCH
 BMP-5 -TNHAIVQTLVHL--MFPDHVVPKPCA--PTKLN AISVL YF--DDSNVILKKYRNMMVVRSCGCH
 BMP-3 -NHATIQSIVRA--VGVPVGIPEPCV--PEKMSSLSILFF--DENKNVILKVYPNMTVESACAR
 MIS -GHVVLL LKMQA--RGAALARPCCV--PTAYAGKLLISLSEER--ISAHVVPNMVA TELCGCR
 Inhibin PGAPPTPAQPS----LLPGAQPCCAALPGTMRPLHVRTTSDGGYFKEYETVPNLL TQHCACI
 Inhibin -SFHSTVINHYMRGHSFANLKSCCV--PTKLRPMSMLY--DDGQNI IKKDIQNMIVEECGCS
 Inhibin -SFHTAVVNQYMRGLNPGT-VNSCCI--PTKLS TMSMLYF--DDEYNIVKRDVPNMIVEECGCA
 TGF- β 1 -TQYSKVALYNG--HNPGASAAPCCV--PQALEPLPIVYV--VGRKPKV--EQLSNMIVRSCKCS
 TGF- β 2 -TQHSRVLSLYNT--INPEASASPCCV--SQDLEPLTILYY--IGKTPKI--EQLSNMIVKSCCKCS
 TGF- β 3 -TTHSTVLGLYNT--LNPEASASPCCV--QDLEPLTILYY--VGRTPKV--EQLSNMVMVKSCKCS

FIG. 3A

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|--------------|-------|-----|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----|---|---|---|---|---|---|---|---|
| SEQ ID NO:28 | GDF-5 | 371 | R | R | K | R | R | A | P | L | A | N | R | Q | G | K | R | P | S | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | 395 | K | N | L | K | A | R | C | S |
| SEQ ID NO:29 | GDF-6 | | R | R | R | R | R | T | A | F | A | S | R | H | G | K | R | H | G | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | | K | S | R | L | R | C | S | | |
| SEQ ID NO:30 | GDF-7 | | R | R | R | R | R | T | A | L | A | G | T | R | G | A | Q | G | S | G | G | G | G | G | G | G | G | G | G | G | G | G | G | G | G | | A | G | R | G | R | R | G | S |

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|-------|-----|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| GDF-5 | 396 | R | K | A | L | H | V | N | F | K | D | M | G | W | D | D | W | I | I | A | P | L | E | Y | E | A | F | H | C | E | G | L | C | E | F | P | L | R | S | H | L | E | P | T | N | H | A | V | I | Q | T | L |
| GDF-6 | | R | K | P | L | H | V | N | F | K | E | L | G | W | D | D | W | I | I | A | P | L | E | Y | E | A | Y | H | C | E | G | V | C | D | F | P | L | R | S | H | L | E | P | T | N | H | A | I | I | Q | T | L |
| GDF-7 | | R | K | S | L | H | V | D | F | K | E | L | G | W | D | D | W | I | I | A | P | L | D | Y | E | A | Y | H | C | E | G | V | C | D | F | P | L | R | S | H | L | E | P | T | N | H | A | I | I | Q | T | L |

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|-------|-----|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| GDF-5 | 447 | M | N | S | M | D | P | E | S | T | P | P | I | C | C | V | P | T | R | L | S | P | I | S | I | L | F | I | D | I | S | A | N | N | V | V | Y | K | Q | Y | E | D | M | V | V | E | S | C | G | C | R |
| GDF-6 | | M | N | S | M | D | P | G | S | T | P | P | S | C | C | V | P | T | K | L | T | P | I | S | I | L | Y | I | D | A | G | N | N | V | V | Y | K | Q | Y | E | D | M | V | V | E | S | C | G | C | R | |
| GDF-7 | | L | N | S | M | A | P | D | A | A | P | A | S | C | C | V | P | A | R | L | S | P | I | S | I | L | Y | I | D | A | A | N | N | V | V | Y | K | Q | Y | E | D | M | V | V | E | A | C | G | C | R | |

FIG.3B

| | | | | | | | | | | | | | | | | | | | | | | |
|-------------------|-----|-----|-----|-----|-----|-----|-----|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------------------|
| GDF-1 | 100 | 33 | 50 | 46 | 44 | 48 | 35 | 27 | 42 | 43 | 46 | 47 | 46 | 42 | 34 | 23 | 37 | 36 | 33 | 32 | 33 | TGF- β 3 |
| GDF-2 | - | 100 | 42 | 47 | 51 | 48 | 31 | 32 | 52 | 51 | 55 | 52 | 55 | 34 | 20 | 20 | 32 | 25 | 26 | 28 | 30 | TGF- β 2 |
| GDF-3 | - | - | 100 | 49 | 49 | 46 | 41 | 33 | 53 | 50 | 53 | 50 | 50 | 42 | 22 | 26 | 42 | 41 | 36 | 31 | 32 | TGF- β 1 |
| GDF-5 | - | - | - | 100 | 86 | 50 | 37 | 33 | 57 | 57 | 51 | 51 | 52 | 47 | 27 | 26 | 40 | 37 | 33 | 34 | 37 | Inhibin β B |
| GDF-6 | - | - | - | - | 100 | 50 | 38 | 34 | 57 | 56 | 53 | 53 | 54 | 46 | 26 | 27 | 43 | 39 | 35 | 36 | 38 | Inhibin β A |
| GDF-7 | - | - | - | - | - | 100 | 37 | 33 | 57 | 57 | 52 | 53 | 52 | 46 | 25 | 26 | 41 | 36 | 36 | 35 | 38 | Inhibin α |
| GDF-8 | - | - | - | - | - | 100 | 27 | 27 | 41 | 38 | 45 | 42 | 42 | 38 | 31 | 26 | 38 | 42 | 34 | 37 | 37 | MIS |
| GDF-9 | - | - | - | - | - | - | 100 | - | 33 | 34 | 31 | 30 | 31 | 29 | 21 | 27 | 30 | 31 | 23 | 25 | 25 | BMP-3 |
| BMP-2 | - | - | - | - | - | - | - | - | 100 | 92 | 61 | 60 | 61 | 48 | 27 | 22 | 42 | 42 | 35 | 34 | 36 | BMP-5 |
| BMP-4 | - | - | - | - | - | - | - | - | - | 100 | 60 | 58 | 59 | 47 | 27 | 22 | 41 | 42 | 34 | 33 | 35 | OP-1 |
| Vgr-1 | - | - | - | - | - | - | - | - | - | - | 100 | 87 | 91 | 44 | 24 | 25 | 44 | 41 | 35 | 37 | 39 | Vgr-1 |
| OP-1 | - | - | - | - | - | - | - | - | - | - | - | 100 | 88 | 42 | 27 | 24 | 43 | 42 | 34 | 38 | 38 | OP-1 |
| BMP-5 | - | - | - | - | - | - | - | - | - | - | - | - | 100 | 43 | 24 | 24 | 43 | 37 | 34 | 35 | 36 | BMP-5 |
| BMP-3 | - | - | - | - | - | - | - | - | - | - | - | - | - | 100 | 30 | 29 | 36 | 37 | 32 | 32 | 32 | BMP-3 |
| MIS | - | - | - | - | - | - | - | - | - | - | - | - | - | - | 100 | 18 | 24 | 25 | 28 | 23 | 25 | MIS |
| Inhibin α | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | 100 | 26 | 25 | 23 | 22 | 24 | Inhibin α |
| Inhibin β A | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | 100 | 63 | 41 | 37 | 36 | Inhibin β A |
| Inhibin β B | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | 100 | 35 | 34 | 37 | Inhibin β B |
| TGF- β 1 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | 100 | 74 | 78 | TGF- β 1 |
| TGF- β 2 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | 100 | 82 | TGF- β 2 |
| TGF- β 3 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | 100 | TGF- β 3 |

FIG. 5A



FIG. 5B



FIG. 5C

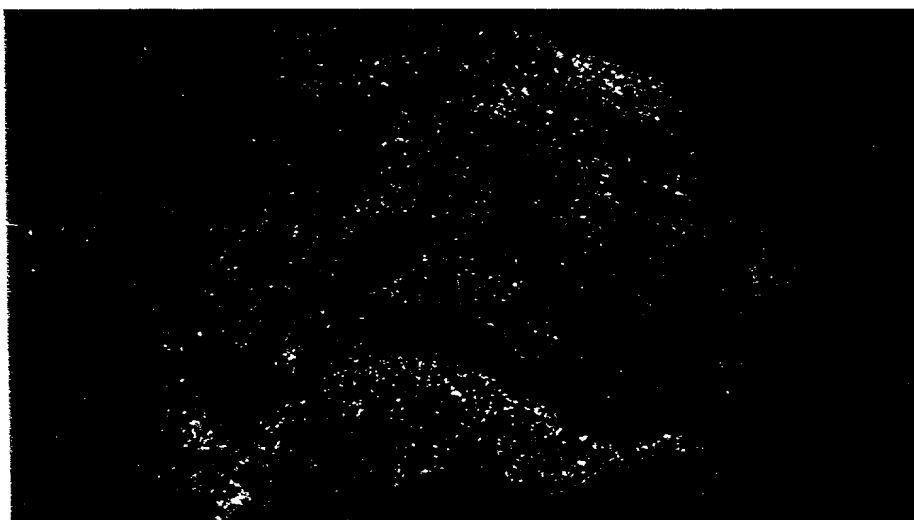


FIG. 5D

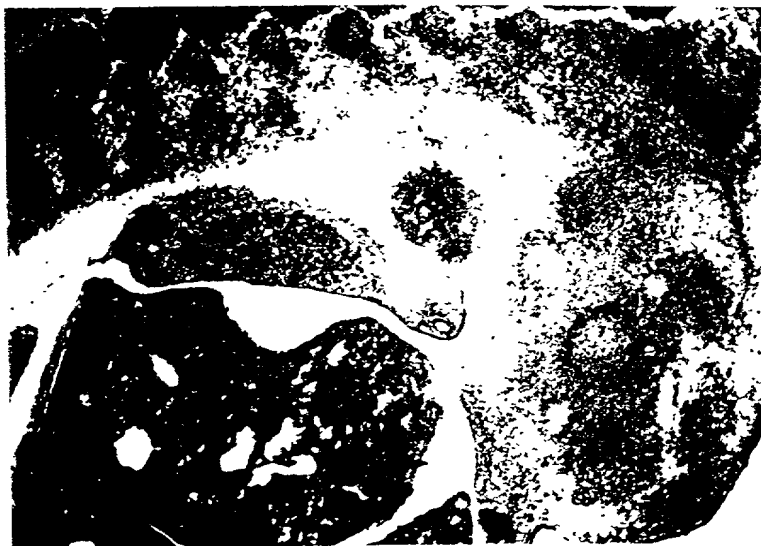


FIG. 5E



FIG. 5F



4 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100



FIG. 6A

FIG. 6B

A high-contrast, black and white photograph of a person's face, heavily shadowed and distorted, appearing to be in a state of distress or agony. The image is characterized by extreme contrast, with deep blacks and bright whites, giving it a graphic, almost abstract quality. The features are partially obscured by shadows, and the overall composition is tightly cropped, focusing on the central part of the face.

FIG. 6C